

Attorney Docket No.: RTS-0139  
Inventors: Baker and Cowser  
Serial No.: 10/035,485  
Filing Date: October 17, 2003  
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#### REMARKS

Claims 1, 2, 4-10 and 12-14 are pending in the instant application. Claims 1, 2, 4-10 and 12-14 have been rejected. Claim 1 has been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### I. Rejection of Claims Under 35 U.S.C. 103(a)

The rejection of claims 1, 2, 4-10 and 12-14 under 35 U.S.C. 103(a) as being unpatentable over Khaw et al. (US Patent No. 6,379,667 B1), in view of Brinckerhoff et al. (1987) and Monia et al. (US Patent No. 6,114,517) has been maintained. The Examiner suggests that it would have been *prima facie* obvious for one of ordinary skill to modify the teachings of Khaw et al. with the teachings of Brinckerhoff et al. and Monia et al. to design the compounds of the instant invention as Khaw et al. teach the general idea of antisense to the gene target of the present invention while Brinckerhoff et al. teach the sequence of the gene and Monia et al. teach the idea of antisense to known target genes, including targeting a coding region of a gene. The Examiner suggests that motivation is provided by the teachings of Khaw et al. in stating

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the use of antisense, while Monia et al. provide the motivation for using modifications to oligonucleotides. Applicants respectfully traverse this rejection.

At the outset, the claims have been amended to recite compounds targeted to a specific nucleobase region within the sequence of SEQ ID NO: 3 to be targeted by antisense. This region is one that was shown in the specification as filed to be successfully targeted by antisense compounds as shown in Table 1. The nucleobase region selected is one that starts at nucleobase 271, listed specifically in Table 1, and one that ends at nucleobase 1351, which is also shown in Table 1 to be targeted by an oligonucleotide of 20 mer that is complementary to nucleobases beginning at 1332 (see Table 1 of the specification as filed). Therefore, Table 1 of the specification as filed clearly defines a region within the coding region that is encompassed by nucleobases 271 through 1351, a region that is also shown to be successfully targeted by many antisense oligonucleotides.

Khaw et al. disclose only the idea of using antisense compounds to inhibit expression of matrix metalloproteinase 1. Nowhere does this patent teach or suggest compounds as claimed which are targeted to a specific nucleobase region of SEQ ID NO: 3.

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Therefore, this primary reference fails to teach or suggest the invention of the amended claims.

The secondary references cited fail to overcome the deficiencies in teaching of the primary reference.

Brinckerhoff et al. (1987) discloses only the sequence of matrix metalloproteinase 1 and its expression in cell lines. Nowhere does this paper teach or suggest compounds as claimed which are targeted to a specific nucleobase region of SEQ ID NO: 3 and which are capable of inhibiting expression of SEQ ID NO: 3. Therefore, this reference, either alone or when combined with the primary reference cited, fails to teach or suggest the invention of the amended claims.

Monia et al. disclose antisense compounds targeted to tumor necrosis factor-alpha signaling molecules. No other antisense compounds of any type are taught or suggested by this patent. Nowhere does this patent teach or suggest compounds as claimed which are targeted to the specific nucleobase region of SEQ ID NO: 3 as now claimed. Therefore, this reference, either considered alone or when combined with the other cited references, fails to teach or suggest the invention of the amended claims.

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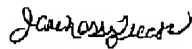
To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to establish a *prima facie* case of obviousness. First, the primary references and the secondary references, when combined, fail to teach or suggest the invention of the amended claims which are compounds targeted to a specific region within the sequence of SEQ ID NO: 3. Further, it is only with the specification in hand that one of skill would be able to know that these particular type of compounds could be used successfully to inhibit expression of SEQ ID NO: 3; the combination of references fail to provide one of skill with an expectation of success without the teachings of the specification in hand. Thus, this combination of prior art fails to establish a *prima facie* case of obviousness and withdrawal of this rejection is respectfully requested.

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## II. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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